Understanding mold illness: how we got here and where are we going

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Don't just call it mold

- Toxigenic sources of inflammation found in water-damaged buildings are fungi, actinomycetes, bacteria, mycobacteria
- Inflammagens are VOC, beta glucans, hemolysins, proteinases and mannosecontaining glycoproteins
- Small particles are far more important than the (larger sized) spores

What do we know about patients with mold illness?

- Illness has a genetic basis
- Physiology involves lack of hypothalamic regulation; deficiency of MSH and VIP
- Illness is readily defined by innate immune responses seen in over 4500 patients
- Prospective acquisition of illness confirms causation; ability to treat the illness is key
- Reproducible appearance of labs with reexposure provides a health index, SAIIE

What do we know about treatment?

- Remove from exposure and begin CSM
- Eliminate biofilm-forming MRCoNS
- Correct MMP9
- Correct autoimmunity: gliadin and cardiolipin
- Correct ADH/osmolality
- Raise VEGF
- Lower C3a and C4a

What do we know about executive cognitive problems in mold illness?

- Markedly present before treatment
- MR spectroscopy shows
 - High lactate in frontal lobes and hippocampus
 - Low ratio glutamate to glutamine (G/G)
- High plasma C4a invariably seen
- To correct C4a use low dose epo
 - Lactate and G/G normalize
 - Symptoms abate in 2 weeks

What do we <u>not</u> know about mold illness?

- Role of HLA DR priming in initial illness
- What is the basis for sicker, quicker?
 - IL-1ra, IL-10, IL-4, IL-8?
 - Toll 2?
 - C-type lectins, dectins, mannose receptors?
- When can we start to use MSH, VIP?
- What does acquired von Willebrand's tell us?

Research needs - I

- HLA in rats, mice and men?
- Animal model must isolate individual contributions and then look for synergism
- Identify sicker, quicker in animals
- Look at cAMP in VIP deficient animals
- Look at absence of downregulation of cytokines in MSH deficiency
- Look for CSM bound to toxin in stool

Research needs - II

- Analysis of gene activation using 124 gene microarray underway; what else?
- "After inhalation of what, does what happen?"
- Genomics, proteomics, metabolomics
- How about glycomics and lipomics?
- Don't forget acidifcation of endosomes required to release HLA in dendrite cell

